REMARKS

The specification has been amended to introduce the subject matter of claim 12 as originally filed. The content of original claim 12 has been introduced as a paragraph as indicated above. No new matter has been introduced, and entry is respectfully requested.

Preliminary comments

Applicants acknowledge the indication of the withdrawal of rejections under 35 USC 112, first paragraph, and the judicially created doctrine of obviousness-type double patenting. Before addressing the outstanding issues, Applicants confirm their understanding that the amendment filed 18 January 2002 (mailed 18 December 2001) has been entered. Additionally, and despite the entry of the Replacement Appeal Brief filed April 10, 2002, prosecution in the instant application has been re-opened.

Objection to the specification

The specification was objected to for failing to provide basis for the subject matter of pending claim 24. Because support for pending claim 24 is found in original claim 12 as filed, the content of original claim 12 has been introduced into page 5 of the specification as indicated above. Applicants respectfully request withdrawal of this objection.

Prior art rejection under 35 U.S.C. § 103

Claims 13, 15, 16 and 18-24 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Spitler (USP 5,738,867) in view of Israeli et al. (USP 5,538,866), Horoszewicz (USP 5,162,504), Andriole et al., the disclosure on pages 10-19 of the instant specification, and McCarley et al. "alone or in combination with" Cruse et al., Kuby, Paul, Grauer et al. (USP 5,250,297), Varki, Linnenbach (USP 5,581,254), Linnenbach et al. (USP 5,668,002) and Sela et al.

Applicants have carefully reviewed the statement of the instant rejection as well as the cited references and traverse the rejection as failing to have presented a *prima facie* case of obviousness.

As an initial matter, Applicants point out that the cited references by Cruse et al., Kuby, Paul, Grauer et al., Varki, Linnenbach, Linnenbach et al., and Sela et al. all appear to relate to the

term "tumor associated antigen", which, for the reasons discussed below, are believed to be irrelevant.

Applicants' review of the statement of the rejection and the cited art suggests that a simple focus be made on the critical issue at hand: whether it would have been obvious to one of ordinary skill at the time of the invention to administer human prostate-specific membrane antigen (PSMA) to a subject to elicit an antitumor immune response against prostate tumors in said subject.

With this focus in mind, it seems critical to examine what was known about PSMA, as reflected in the cited references. While Spitler, as recognized in the Action, is silent with respect to PSMA, Israeli et al. and Horoszewicz are wholly, or in great part, directed to PSMA. And while both Israeli et al. and Horoszewicz describe the production of antibodies against PSMA and even the administration of such antibodies to subjects for various reasons, **neither of the references teaches, suggests, or otherwise indicates the concept of using PSMA to elicit an antitumor immune response against prostate tumors.**

Additionally, and while both Israeli et al. and Horoszewicz mention the presence of PMSA on prostate tumor cells, neither of the references teaches, suggests, or otherwise indicates the concept of PMSA as a "tumor associated antigen". Horoszewicz does note repeatedly, however, that a monoclonal antibody against PMSA (7E11-C5, also discussed in Israeli et al. in column 2) stains the periphery of malignant prostate epithelial cells as well as normal prostate epithelial cells and benign prostatic hypertrophy cells (see column 6, lines 25-31 and lines 56-58; and column 10,lines 42-60).[1] But this of course does not lead the artisan of ordinary skill to the use of PMSA to elicit an antitumor response.

The lack of any indication of PMSA as a "tumor associated antigen" leads to the identification of the first deficiency of the instant rejection: no motivation to combine with the teachings of Spitler. As recognized in the Action, Spitler teaches the use of "tumor associated antigens" as antitumor vaccines. But contrary to the Action's reference to the Summary of the

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[1] Therefore, the issue of whether PMSA is specific to prostate tumor cells or also found in normal prostate cells is moot. Accordingly, it is believed that the cited references by Cruse et al., Kuby, Paul, Grauer et al., Varki, Linnenbach, Linnenbach et al., and Sela et al. need not be addressed in detail because their inclusion in the instant rejection appears either 1) to be directed at this mooted issue or 2) to be directed to making a point already made (and thus cumulative with) the teachings of Horoszewicz.

Invention in Spitler (column 2, lines 15-27), Spitler does not teach the use of "prostate antigens". To the contrary, that passage states that the "tumor associated antigen" known as "GA733-2, *associated with tumors of the gastrointestinal tract, prostate, cervix, ovary, bladder, lung, breast, colorectum, and pancreas*" (emphasis added) may be used in accordance with the teachings of Spitler. Applicants respectfully submit that a single antigen found on tumors of these various and diverse tissues is **not** a teaching of "prostate antigens" as alleged by the Examiner.

Otherwise, Spitler does not mention "prostate" or any variation thereof. As such, where is the teaching, suggestion, indication, motivation, or guidance leading the artisan of ordinary skill to the use of PMSA in the teachings of Spitler? Without some indication leading the artisan to such a modification of Spitler, there is no motivation to support a *prima facie* assertion of obviousness, and the instant rejection appears to be based upon impermissible hindsight reconstruction. The mere fact that Israeli et al. and Horoszewicz disclose various teachings related to PMSA is insufficient to avoid hindsight. There must be some motivation for the modification of Spitler with the teachings of Israeli et al. and Horoszewicz.

The teachings of Andriole et al. and McCarley et al. do not offer anything to remedy this critical deficiency in the instant rejection. Both references fail to even mention PMSA or the use of antigens to generate an antitumor immune response. To the extent that McCarley et al. teach that "prostate antigens are not usually tumor specific" as alleged in the Action, Applicants respectfully point out that the specificity of PMSA is already addressed in Horoszewicz as discussed above.

Similarly, no part of the discussion on pages 10-19 of the instant specification teach or suggest any prior knowledge of the use of PMSA to elicit an antitumor immune response.

And finally, the references by Cruse et al., Kuby, Paul, Grauer et al. (USP 5,250,297), Varki, Linnenbach (USP 5,581,254), Linnenbach et al. (USP 5,668,002) and Sela et al., alone or in any combination with each other or the references discussed above, remedies the critical deficiency identified in the instant rejection.

Applicants note that in light of the critical lack of motivation, as required by MPEP 2143.01 and the cases cited therein, there can be no *prima facie* assertion of obviousness. Applicants therefore respectfully request that this rejection be withdrawn.

Conclusion

In light of the above amendments and remarks, Applicant respectfully submits that claims 13, 15, 16, and 18-24 may be indicated as allowable, and early indication to that effect is urged. The Examiner is welcome to contact the undersigned if he determines that further discussions would prove useful.

In the event that the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **204372000301**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: October 15, 2002 By: _____

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